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Docket No.: PF-0519-1-DIV

OCT 02 2000

selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, a fragment of SEQ ID NO:2, a fragment of SEQ ID NO:4, a fragment of SEQ ID NO:6, and a fragment of SEQ ID NO:8.

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9. **(Reiterated)** An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 7.

10. **(Reiterated)** An expression vector comprising at least a fragment of the polynucleotide of claim 3.

11. **(Reiterated)** A host cell comprising the expression vector of claim 10.

12. **(Reiterated)** A method for producing a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, a fragment of SEQ ID NO:1, a fragment of SEQ ID NO:3, a fragment of SEQ ID NO:5, and a fragment of SEQ ID NO:7, the method comprising the steps of:

- a) culturing the host cell of claim 11 under conditions suitable for the expression of the polypeptide; and
- b) recovering the polypeptide from the host cell culture.

19. **(Reiterated)** A method for detecting a polynucleotide encoding the polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, a fragment of SEQ ID NO:1, a fragment of SEQ ID NO:3, a fragment of SEQ ID NO:5, and a fragment of SEQ ID NO:7 in a biological sample, the method comprising the steps of:

- (a) hybridizing the polynucleotide of claim 6 to at least one of the nucleic acids in the biological sample, thereby forming a hybridization complex; and
- (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of the polynucleotide encoding the polypeptide in the biological sample.

20. **(Reiterated)** The method of claim 19 wherein the nucleic acids of the biological sample are amplified by the polymerase chain reaction prior to the hybridizing step.

21. **(Once amended)** A purified polypeptide comprising an amino acid sequence selected from the group consisting of:

- B1  
m  
C1
- a) an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5;
  - b) a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:3 or SEQ ID NO:5;
  - c) a biologically-active fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5 having apoptotic activity; and
  - d) an immunogenic fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5 comprising at least 30 contiguous amino acid residues.

22. **(Reiterated)** An isolated polypeptide of claim 21, having a sequence of SEQ ID NO:3 or SEQ ID NO:5.

23. **(Reiterated)** An isolated polynucleotide encoding a polypeptide of claim 21.

24. **(Reiterated)** A method for producing a polypeptide of claim 21, the method comprising:

- a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 21; and
- b) recovering the polypeptide so expressed.

25. **(Reiterated)** A method of claim 24, wherein the polypeptide has the sequence of SEQ ID NO:3 or SEQ ID NO:5.

26. **(Reiterated)** An isolated antibody which specifically binds to a polypeptide of claim 21.

B2  
m  
C1

27. **(Once amended)** A [pharmaceutical] composition comprising [an effective amount of] a polypeptide of claim 21 and a pharmaceutically acceptable excipient.

B2  
C1  
28. **(Once amended)** A [pharmaceutical] composition of claim 27, wherein the polypeptide has the sequence of SEQ ID NO:3 or SEQ ID NO:5.

29. **(Reiterated)** A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 21, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 21 to a compound; and
- b) detecting agonist activity in the sample.

30. **(Reiterated)** A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 21, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 21 to a compound; and
- b) detecting antagonist activity in the sample.

B3  
31. **(Once amended)** A [pharmaceutical] composition comprising the antibody of claim 26 in conjunction with a suitable pharmaceutical carrier.

32. **(Reiterated)** A method of preparing a polyclonal antibody with the specificity of the antibody of claim 26 comprising:

- a) immunizing an animal with the polypeptide of SEQ ID NO:3 or SEQ ID NO:5 or an antigenically-effective fragment thereof under conditions to elicit an antibody response;
- b) isolating animal antibodies; and
- c) screening the isolated antibodies with the polypeptide thereby identifying a polyclonal antibody binds specifically to the polypeptide of SEQ ID NO:3 or SEQ ID NO:5.

33. **(Reiterated)** An antibody produced by a method of claim 32.

B4  
34. **(Once amended)** A [pharmaceutical] composition comprising the antibody of claim 33 in conjunction with a suitable pharmaceutical carrier.

35. **(Reiterated)** A method of making a monoclonal antibody with the specificity of the antibody of claim 26 comprising:

- a) immunizing an animal with the polypeptide of SEQ ID NO:3 or SEQ ID NO:5 or an

- antigenically-effective fragment thereof under conditions to elicit an antibody response;
- b) isolating antibody producing cells from the animal;
  - c) fusing the antibody producing cells with immortalized cells in culture to form monoclonal antibody-producing hybridoma cells;
  - d) culturing the hybridoma cells; and
  - e) isolating from the culture monoclonal antibodies which binds specifically to the polypeptide of SEQ ID NO:3 or SEQ ID NO:5.

36. **(Reiterated)** A monoclonal antibody produced by a method of claim 35.

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35 37. **(Once amended)** A [pharmaceutical] composition comprising the antibody of claim 36 in conjunction with a suitable pharmaceutical carrier.

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38. **(Reiterated)** The antibody of claim 26, wherein the antibody is:

- (a) a chimeric antibody;
- (b) a single chain antibody;
- (c) a Fab fragment; or
- (d) a F(ab')<sub>2</sub> fragment.

39. **(Reiterated)** A method for detecting polypeptide of SEQ ID NO:3 or SEQ ID NO:5 in a sample comprising the steps of:

- a) combining the antibody of claim 26 with a sample under conditions to allow specific binding; and
- b) detecting specific binding, wherein specific binding indicates the presence of polypeptide of SEQ ID NO:3 or SEQ ID NO:5 in the sample.

40. **(Reiterated)** A method of using an antibody to purify polypeptide of SEQ ID NO:3 or SEQ ID NO:5 from a sample, the method comprising:

- a) combining the antibody of claim 26 with a sample under conditions to allow specific binding; and
- b) separating the antibody from the protein, thereby obtaining purified polypeptide of SEQ ID NO:3 or SEQ ID NO:5.

Please add the following new claims:

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B6  
- 41. A method of screening for a compound that specifically binds to the polypeptide of claim 21, said method comprising the steps of:

- a) combining the polypeptide of claim 21 with at least one test compound under suitable conditions; and
- b) detecting binding of the polypeptide of claim 21 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 21.

42. A method of screening for a compound that modulates the activity of the polypeptide of claim 21, said method comprising:

- a) combining the polypeptide of claim 21 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 21;
  - b) assessing the activity of the polypeptide of claim 21 in the presence of the test compound; and
  - c) comparing the activity of the polypeptide of claim 21 in the presence of the test compound with the activity of the polypeptide of claim 21 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 21 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 21. –
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#### REMARKS

Initially, it is noted that the Examiner failed to completely examine Applicants' invention. Specifically, Applicants object to the Examiner's failure to obtain the parent application and references therein prior to preparing this Office Action. Therefore, Applicants insist that the Examiner do so, that she fully consider the priority grant regarding claims 21, 22, 27, and 28, as well as fully consider the references cited in the parent application and listed on the Form 1449. In no case should any rejection in a subsequent Office Action relating to the Examiner's failure to obtain the parent file be made final.

#### Applicants' invention

The invention is based, *inter alia*, on the discovery of new human apoptosis associated proteins